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13. Abstract (Maximum 200 Words) (abstract should contain no proprietary or confidential information) Over the past year, we have selected 123 breast cancer cases diagnosed 1997-1999 and 217 matched controls from the mammography database at the Mayo Clinic. Controls were matched to cases on age, race, menopausal status, distribution of mammograms and month of last appointment for mammogram. All mammograms over the last 10 years were obtained on these women, digitized, and stored in a format that can be read by our breast density estimation software. Risk factor information was abstracted from charts on all these women, including weight information at times of mammograms, hormone replacement therapy use, tamoxifen, raloxifene medications, family history, alcohol and smoking information. We will obtain parity and age at first birth from the mammography database. We have estimated breast density on the oldest mammogram from both cases and controls, using our semi-automated software and using a subjective categorical estimate. We have begun preliminary analyses to examine the association of percent breast density and absolute dense area (using the oldest mammogram) with breast cancer risk. Next winter, we will continue these analyses investigating the change in density over time and breast cancer risk. Also, we will continue to retrospectively identify and collect breast cancer cases and controls from the mammography database. Our goal is to collect at least 200 cases and 400 controls over the next two years.				
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Introduction

The interindividual variability in breast tissue on mammographic images, as defined by several measures of mammographic breast density, has been shown to be a major risk factor for breast cancer with three to five-fold increases in risk associated with densities greater than 50% (Boyd, 1998). To date, all studies of breast density and cancer have involved only a single measure of breast density taken between 1-16 years before diagnosis. However, as a women ages, her breast density changes, with the greatest changes reported at menopause. It is not known whether a change in breast density or the rate at which this change occurs is associated with breast cancer risk. Our hypothesis is that women who have a slower rate of change from dense to fatty tissue will be at a higher risk for breast cancer than women who change at a greater rate.

To address this hypothesis, over the past year, we have designed and implemented a case-control study, which aims to identify incident cases of breast cancer that have occurred between years 1997-2001 in women ages 50 and older, living within 120 miles of the Mayo Clinic, that were screened over the past ten years at the Mayo Clinic. We also have started to collect controls, matched on age, race, menopausal status, distribution of mammograms and month of last appointment for mammogram. We will collect mammograms and risk factor information on all women over the last 10 years using mammography database and medical record information. The mammographic images will be digitized and breast density (both percent density and total area of density) will be estimated using a semi-automated computer algorithm that has been found to be reliable in several studies (Byng, 1994; Byng, 1996). The absolute change and rate of change for each individual will be computed and compared between breast cancer cases and controls, adjusting for baseline breast density and other breast cancer risk factors.

To date, we have ascertained all cases between the years 1997-1999, selected matched controls also having a mammogram during these years, abstracted chart data on all these individuals, collected and digitized their mammograms and are beginning preliminary analyses on these individuals. We are currently selecting cases and controls from the year 2000.

If a change of breast density over time does influence breast cancer risk, these results will provide an important new avenue of research in breast cancer etiology, including identifying high risk individuals for prevention and examining agents that could affect this progression.

Body

The goal of our study is to examine the association between change in breast density over time and breast cancer risk. The emphasis of the first year of this four year study is to ascertain cases and controls from the years 1997-1999, collect their mammograms over the past 10 years, abstract chart data and obtain other data from the mammography database. We are on task to date, and are beginning to collect cases and controls from the year 2000. Below is a detailed description of the activities in the first year of our study.

We first selected cases and controls eligible by our defined criteria. For cases, eligibility criteria included women aged 50 years or greater, living within the geographic region of the Mayo Health System (~120 miles), who had two or more mammograms performed within the ten years prior to their period of ascertainment. Additionally, at least two of these mammograms must have been performed three years prior to the year of ascertainment. Control women were age-matched within 6 months of the case, will be of the same race and menopausal status, had the same distribution of screening mammograms in the last ten years and had been seen in the Mammography Clinic for a screening mammogram the same month of diagnosis of the breast cancer case. We identified cases and controls through the computerized mammography and pathology databases at the Mayo Clinic, which include detailed clinical and self-reported interview data obtained on women as they come for their mammography appointments.

Initially, we identified a total of 189 potential breast cancer cases meeting these eligibility criteria over this three year period. However, there were several exclusions that occurred, bringing our number down to 123. They included the following listed in the table below:

Reasons for Exclusion as a Case

Previous breast cancer (not an incident case)	5
Bilateral breast cancer	9
No mammogram available for opposite breast-noncancer side used in evaluation of change	25
<ul style="list-style-type: none"> • Unilateral mastectomy or implants--16 • View can't be located--9 	
Only a benign lesion—not a breast cancer	27

Controls were next ascertained for these 123 women, based on the matching criteria specified above. In the matching procedure, 4 cases did not match and therefore, could not be used in analyses. Also there were problems ascertaining 2 controls on every case, thus, only one control was available for 23 of the cases. The primary reason for exclusion was a history of breast cancer in a control.

For all these women, risk factor data (including BMI at each mammogram date) was abstracted from the medical histories in identical manner to the cases. An abstraction form is included in the appendix. Also, mammograms were digitized and stored on all cases and controls.

In regard to our statement of work, we have completed task 1; task 2 for the cases in years 1997-1999; task 3 for the controls in the years 1997-1999; and task 4 for cases and controls in years 1997-1999. Although not part of our proposed statement of work, we have also began preliminary analyses to examine the association of percent breast density and breast area in the oldest mammogram with breast cancer risk. We expect to complete these by September of 2001 and submit an abstract to the AACR and/or ASPO conferences.

Research Accomplishments

- Selected breast cancer cases between years 1997-1999, abstracted chart data on these women and obtained and digitized mammograms.
- Selected matched controls for cases diagnosed between 1997-1999, abstracted chart data on these women and obtained and digitized mammograms.
- Estimated percent breast density on earliest mammogram from both cases and controls.
- Performed intra and interreliability studies to evaluate performance of the computer-assisted method.
- Performing preliminary analyses to investigate the breast density and breast cancer association.
- Currently, selecting cases and controls from year 2000 for study.

Reportable Outcomes

None to date. The first year of our study has only involved data collection.

Conclusions

The first year of our study has been productive, designing the protocol, ascertaining cases and controls, abstracting data, digitizing mammograms, estimating breast density and initiating analyses. The only deviation from our Statement of Work is our decision to perform analyses of percent breast density and breast area on the earliest mammograms with breast cancer risk. We view these analyses as important, to emphasize that are data are consistent with those in the literature.

Breast density has consistently been seen to be associated with breast cancer, but there is little understanding of the mechanism. Understanding the association between the dynamic change in breast density over time and breast cancer risk will provide another clue into the etiology of breast cancer as well as target women for prevention efforts.

References

- Boyd NF, Lockwood GA, Byng JW, Tritchler DL, Yaffe M.J. Mammographic densities and breast cancer risk. *Cancer Epidemiol Biomark Prev* 1998;7:1133-1144.
- Byng J.W, Boyd N.F, Little L, Lockwood G, Fishell E, Jong RA., Yaffe MJ. Symmetry of projection in the quantitative analysis of mammographic images. *European J Cancer Prev* 1996;5:319-327.
- Byng JW, Boyd NF, Fishell E, Jong RA, Yaffe MJ. The quantitative analysis of mammographic densities. *Phys Med Biol* 1994;39:1629-1638.

Today's Date: __/__/____

Clinic Number: __ - ____ - ____

Natural History of Breast Density Chart Review

Please complete all applicable fields below for both case and control women.

Breast Cancer Validation

1. Does patient have primary breast cancer?

☐ Yes ☐ No (Go to Page 2, Q. 2)



Date of breast cancer diagnosis: __/__/____

Side of breast with cancer: ☐ Right ☐ Left

Quadrant: Upper Outer
 Upper Inner
 Lower Inner
 Lower Outer

Size of tumor: _____

Tumor: T_____

Nodes: N_____

Metastasis: M_____

Stage of Tumor: 0
 I
 IIA
 IIB
 IIIA
 IIIB
 IV

Grade: _____

Receptor Status: ER+/PR+
 ER+/PR-
 ER-/PR+
 ER-/PR-

Histology: _____

Any breast cancer before primary cancer diagnosis? ☐ Yes ☐ No

Today's Date: __/__/____

Clinic Number: __ - ____ - ____

Corresponding weight and height for date of each mammogram since 1989

For each mammogram date, find the weight and height measurement in the chart within two months of the date. If the information is unavailable, please leave blank. Please enter height in cm and weight in kg.

2. Date Mammogram 1: __/__/____ Height: ____cm Weight: ____kg

3. Date Mammogram 2: __/__/____ Height: ____cm Weight: ____kg

4. Date Mammogram 3: __/__/____ Height: ____cm Weight: ____kg

5. Date Mammogram 4: __/__/____ Height: ____cm Weight: ____kg

6. Date Mammogram 5: __/__/____ Height: ____cm Weight: ____kg

7. Date Mammogram 6: __/__/____ Height: ____cm Weight: ____kg

8. Date Mammogram 7: __/__/____ Height: ____cm Weight: ____kg

9. Date Mammogram 8: __/__/____ Height: ____cm Weight: ____kg

10. Date Mammogram 9: __/__/____ Height: ____cm Weight: ____kg

11. Date Mammogram 10: __/__/____ Height: ____cm Weight: ____kg

12. Date Mammogram 11: __/__/____ Height: ____cm Weight: ____kg

Today's Date: __/__/____

Clinic Number: _ - ____ - ____

Hormone Replacement Therapy, Anti-estrogen Therapy

13. Did the patient take hormone replacement therapy? ☐ Yes ☐ No (Go to Q. 14)



Date Started: __/__/____	Type _____
Date Stopped: __/__/____	Dose _____
<input type="checkbox"/> Current user	
Date Started: __/__/____	Type _____
Date Stopped: __/__/____	Dose _____
Date Started: __/__/____	Type _____
Date Stopped: __/__/____	Dose _____
Date Started: __/__/____	Type _____
Date Stopped: __/__/____	Dose _____
Date Started: __/__/____	Type _____
Date Stopped: __/__/____	Dose _____

14. Did the patient take tamoxifen?

☐ Yes ☐ No (Go to Q. 15)



Date Started: __/__/____	Dose _____
Date Stopped: __/__/____	
<input type="checkbox"/> Current user	
Date Started: __/__/____	Dose _____
Date Stopped: __/__/____	

15. Did the patient take raloxifene (evista)?

☐ Yes ☐ No (Go to Q. 16)



Date Started: __/__/____	Dose _____
Date Stopped: __/__/____	
<input type="checkbox"/> Current user	
Date Started: __/__/____	Dose _____
Date Stopped: __/__/____	

Today's Date: __/__/----

Clinic Number: __-____-____

Family History

16. Did the patient have a family history of breast or ovarian cancer in a first degree relative?

Relationship _____ Type of Cancer: _____

Comment: _____

Relationship _____ Type of Cancer: _____

Comment: _____

Relationship _____ Type of Cancer: _____

Comment: _____

Relationship _____ Type of Cancer: _____

Comment: _____

Relationship _____ Type of Cancer: _____

Comment: _____

Relationship _____ Type of Cancer: _____

Comment: _____

(1=Breast, 2=Ovarian, 3=Both, 4=Other, 5=No, 6=Don't Know)

Smoking and Alcohol Use

17. Did the patient drink alcohol during her lifetime?

- ☐ Never drinker
- ☐ Less than weekly
- ☐ Weekly
- ☐ Daily
- ☐ Don't Know

Additional Comments _____

18. Did the patient change her alcohol consumption over the past years?

- ☐ Yes
- ☐ No
- ☐ Don't Know

If Yes, Stop Year _____ Start Year _____

Specify _____

Additional Comments _____

19. Did the patient smoke during her lifetime?

- ☐ Never smoker
- ☐ Former smoker
- ☐ Current smoker
- ☐ Don't Know

19a. Cigarettes per Day: _____

Comment: _____

20. Did the patient change her smoking status over the past years?

- ☐ Yes
- ☐ No
- ☐ Don't Know

If Yes, Stop Year _____ Start Year _____

Specify _____

Additional Comments _____